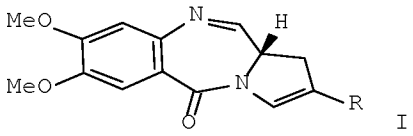
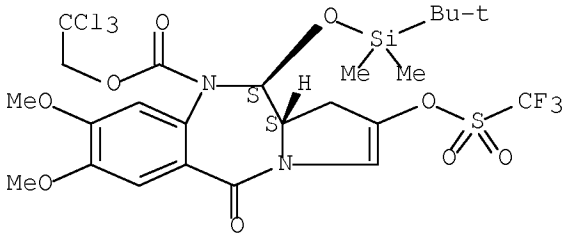
L15 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2007:360773 CAPLUS Full-text
DN 147:9874
TI Parallel Synthesis of a Novel C2-Aryl Pyrrolo[2,1-c][1,4]benzodiazepine (PBD) Library
AU Antonow, Dyeison; Cooper, Nectaroula; Howard, Philip W.; Thurston, David E.
CS Spirogen Limited, London, NW1 0NH, UK
SO Journal of Combinatorial Chemistry (2007), 9(3), 437-445
CODEN: JCCHFF; ISSN: 1520-4766
PB American Chemical Society
DT Journal
LA English
OS CASREACT 147:9874
GI



I

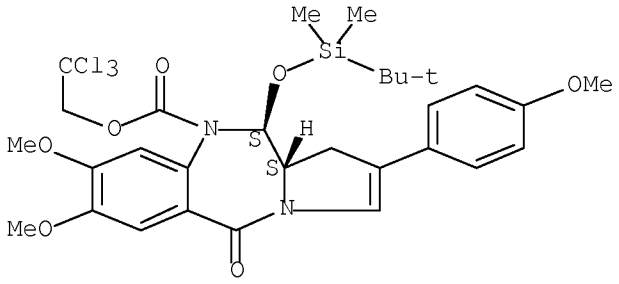
AB A 66-membered library of C2-aryl pyrrolo[2,1-c][1,4]benzodiazepines I [R = Ph, 4-MeOC6H4, 3-H2NC6H4, 2-F3CC6H4, 4-(4-methyl-1-piperazinyl)phenyl, 2-thienyl, 4-pyridyl, 2-naphthyl, etc.] has been successfully prepared by parallel synthesis via Suzuki coupling using polystyrene-bound Pd(PPh3)4 as catalyst and polystyrene-bound diethanolamine as scavenger under microwave irradiation Library members were obtained in sufficient yields (up to 91%) and purity (85-98% crude) for biol. evaluation.
IT 864754-74-5P 937720-37-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(parallel synthesis of aryl-substituted pyrrolo[2,1-c][1,4]benzodiazepine library via Suzuki coupling under microwave irradiation)
RN 864754-74-5 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-10(5H)-carboxylic acid, 11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-11,11a-dihydro-7,8-dimethoxy-5-oxo-2-[[(trifluoromethyl)sulfonyl]oxy]-, 2,2,2-trichloroethyl ester, (11S,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 937720-37-1 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-10(5H)-carboxylic acid, 11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-11,11a-dihydro-7,8-dimethoxy-2-(4-methoxyphenyl)-5-oxo-, 2,2,2-trichloroethyl ester, (11S,11aS)- (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2006:1124678 CAPLUS Full-text
DN 145:455035
TI Preparation of pyrrolobenzodiazepine derivatives for treatment of proliferative diseases
IN Gregson, Stephen John; Howard, Philip Wilson; Chen, Zhizhi
PA Spirogen Limited, UK
SO PCT Int. Appl., 77pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2006111759	A1	20061026	WO 2006-GB1456	20060421
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	AU 2006238686	A1	20061026	AU 2006-238686	20060421
	CA 2604805	A1	20061026	CA 2006-2604805	20060421
	GB 2439881	A	20080109	GB 2007-20721	20060421
	EP 1879901	A1	20080123	EP 2006-726846	20060421
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
	JP 2008536905	T	20080911	JP 2008-507165	20060421
	IN 2007DN07862	A	20071109	IN 2007-DN7862	20071011
	US 20080167293	A1	20080710	US 2007-911890	20071018
	MX 2007013039	A	20080313	MX 2007-13039	20071019
	CN 101171257	A	20080430	CN 2006-80015716	20071108
	KR 2008004618	A	20080109	KR 2007-727047	20071120
PRAI	GB 2005-8084	A	20050421		
	GB 2005-22746	A	20051107		
	WO 2006-GB1456	W	20060421		

OS CASREACT 145:455035; MARPAT 145:455035
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. with general formula I [wherein: R2 = (un)substituted aryl; R6 and R9 = independently H, R, OH, OR, SH, SR, NH2, NHR, NRR', nitro, Me3Sn, or halo, where R and R' = independently (un)substituted alkyl, heterocyclyl, or aryl; R7 = H, R, OH, OR, SH, SR, NH2, NHR, NHRR', nitro, Me3Sn, or halo; Z = alkylene; X = O, S, or NH; n = 2 or 3] or pharmaceutically acceptable salts or solvates thereof are prepared for the treatment of proliferative diseases. For example, compound II•2Na was prepared in a multi-step synthesis. II•2Na showed IC50 of 1.5 nM in the In Vitro cytotoxicity test with K562 human chronic myeloid leukemia cells.

IT 864754-61-0P 864754-66-5P 913262-19-8P
913262-21-2P 913262-23-4P 913262-24-5P
913262-26-7P 913262-28-9P 913262-38-1P

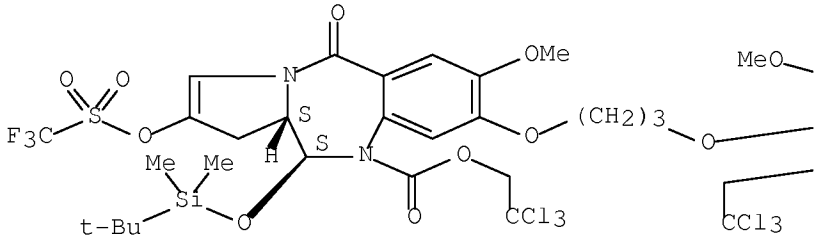
913262-39-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)(preparation of pyrrolobenzodiazepine derivs. for treatment of proliferative diseases)

RN 864754-61-0 CAPLUS

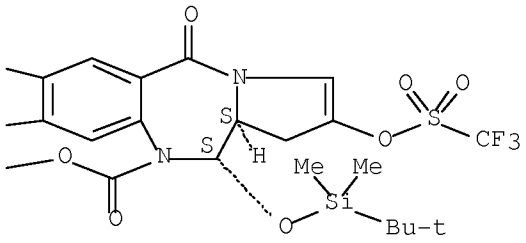
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-10(5H)-carboxylic acid, 8,8'-[1,3-propanediylbis(oxy)]bis[11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-11,11a-dihydro-7-methoxy-5-oxo-2-[[(trifluoromethyl)sulfonyl]oxy]-, bis(2,2,2-trichloroethyl) ester, (11S,11'S,11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B

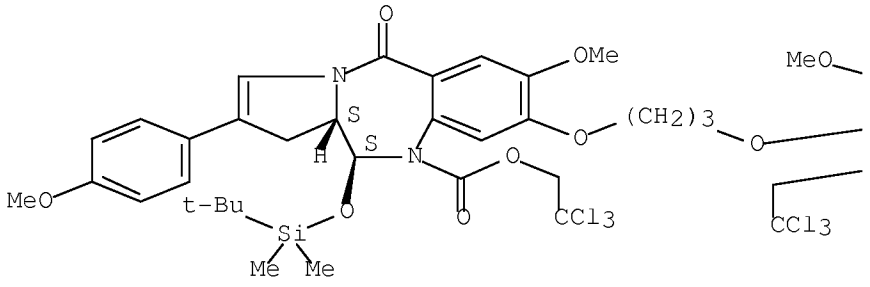


RN 864754-66-5 CAPLUS

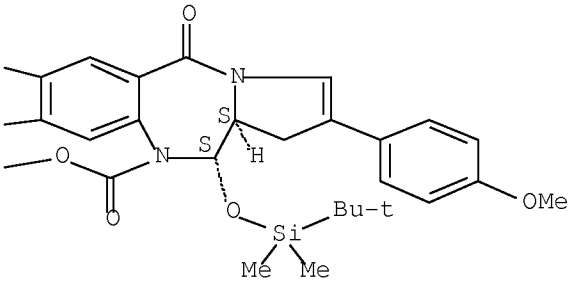
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-10(5H)-carboxylic acid, 8,8'-[1,3-propanediylbis(oxy)]bis[11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-11,11a-dihydro-7-methoxy-2-(4-methoxyphenyl)-5-oxo-, bis(2,2,2-trichloroethyl) ester, (11S,11'S,11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



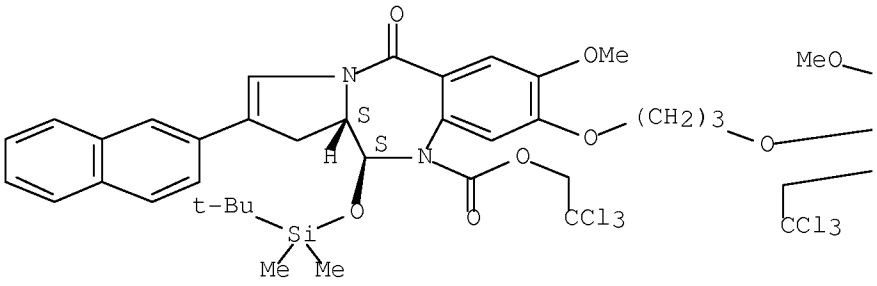
PAGE 1-B



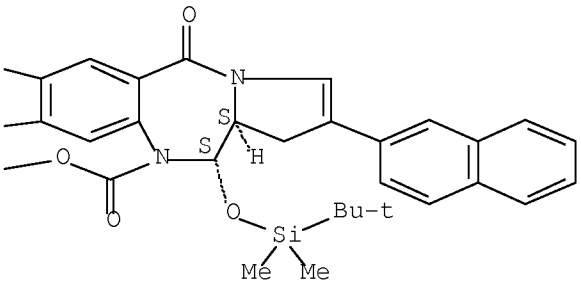
RN 913262-19-8 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-10(5H)-carboxylic acid, 8,8'-[1,3-propanediylbis(oxy)]bis[11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-11,11a-dihydro-7-methoxy-2-(2-naphthalenyl)-5-oxo-, bis(2,2,2-trichloroethyl) ester, (11S,11'S,11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

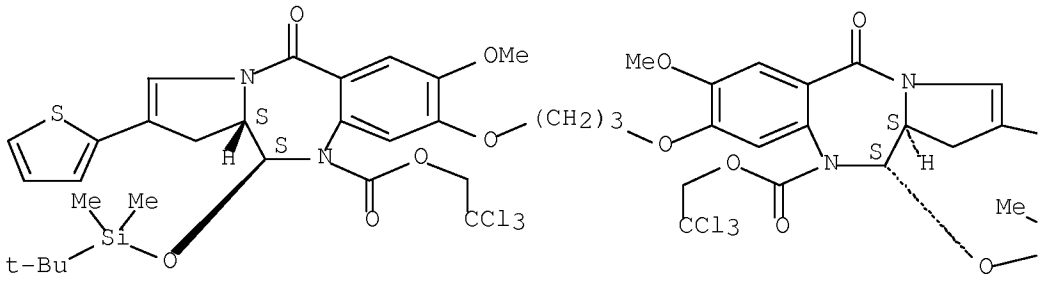


RN 913262-21-2 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-10(5H)-carboxylic acid, 8,8'-[1,3-propanediylbis(oxy)]bis[11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-11,11a-dihydro-7-methoxy-5-oxo-2-(2-

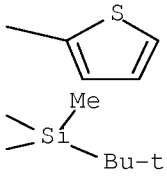
thienyl)-, bis(2,2,2-trichloroethyl) ester, (11S,11'S,11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



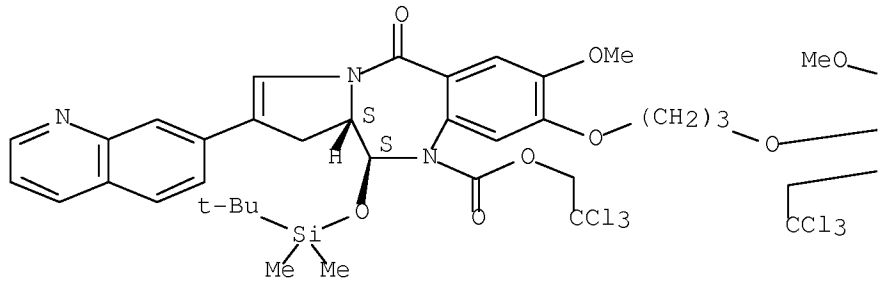
PAGE 1-B



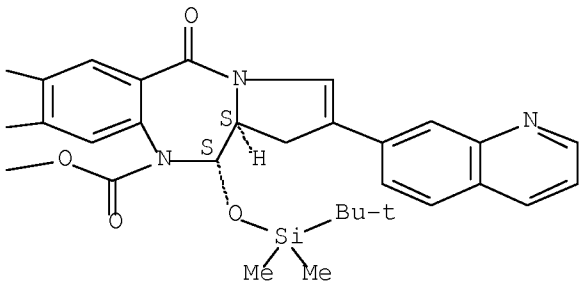
RN 913262-23-4 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-10(5H)-carboxylic acid, 8,8'-[1,3-propanediylbis(oxy)]bis[11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-11,11a-dihydro-7-methoxy-5-oxo-2-(7-quinolinyl)-, bis(2,2,2-trichloroethyl) ester, (11S,11'S,11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



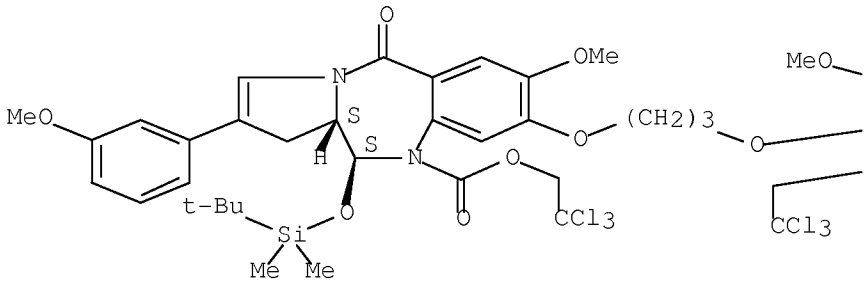
PAGE 1-B



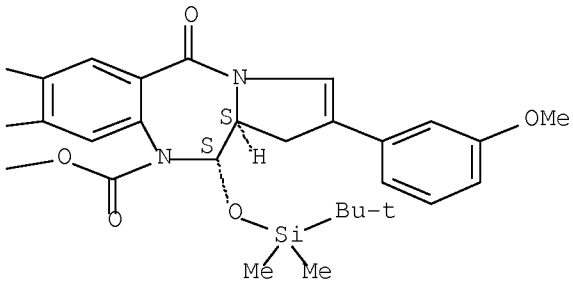
RN 913262-24-5 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-10(5H)-carboxylic acid, 8,8'-[1,3-propanediylbis(oxy)]bis[11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-11,11a-dihydro-7-methoxy-2-(3-methoxyphenyl)-5-oxo-, bis(2,2,2-trichloroethyl) ester, (11S,11'S,11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



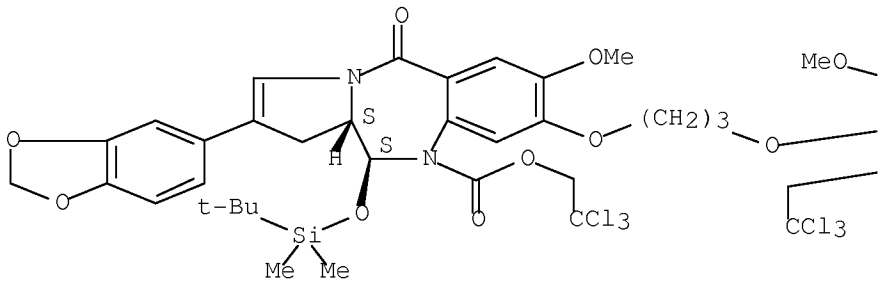
PAGE 1-B



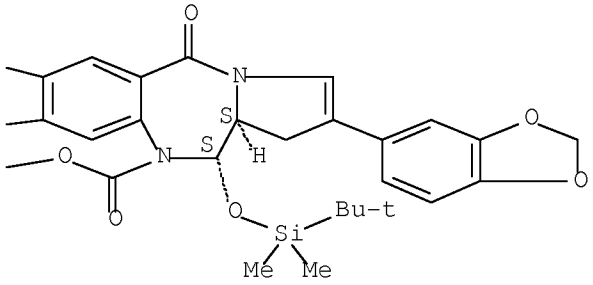
RN 913262-26-7 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-10(5H)-carboxylic acid, 8,8'-[1,3-propanediylbis(oxy)]bis[2-(1,3-benzodioxol-5-yl)-11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-11,11a-dihydro-7-methoxy-5-oxo-, bis(2,2,2-trichloroethyl) ester, (11S,11'S,11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



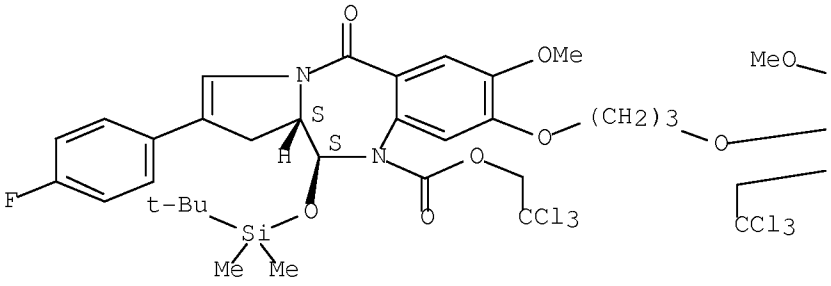
PAGE 1-B



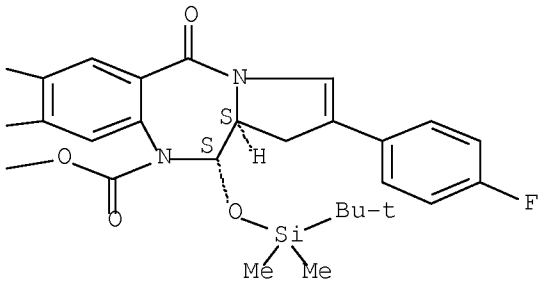
RN 913262-28-9 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-10(5H)-carboxylic acid, 8,8'-[1,3-propanediylbis(oxy)]bis[11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-2-(4-fluorophenyl)-11,11a-dihydro-7-methoxy-5-oxo-, bis(2,2,2-trichloroethyl) ester, (11S,11'S,11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



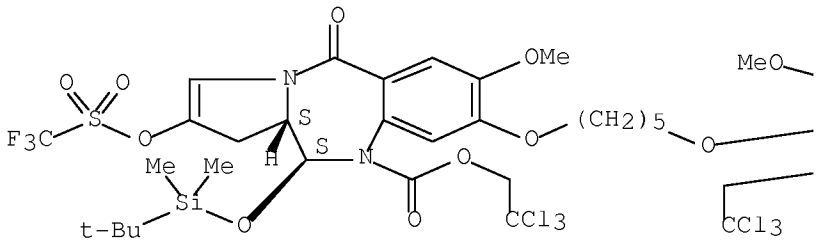
PAGE 1-B



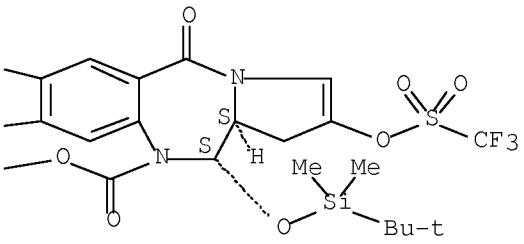
RN 913262-38-1 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-10(5H)-carboxylic acid, 8,8'-[1,5-pentanediylbis(oxy)]bis[11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-11,11a-dihydro-7-methoxy-5-oxo-2-[[(trifluoromethyl)sulfonyl]oxy]-, bis(2,2,2-trichloroethyl) ester, (11S,11'S,11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



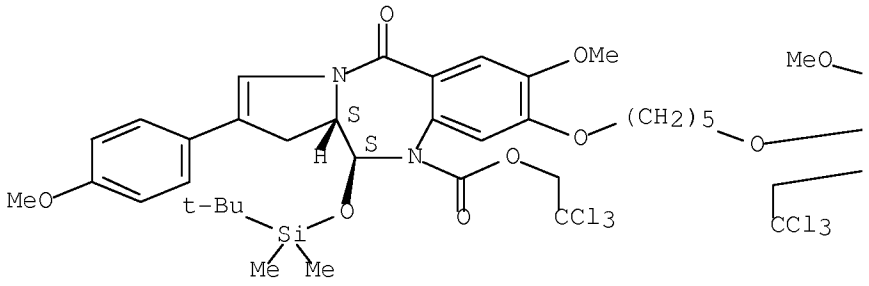
PAGE 1-B



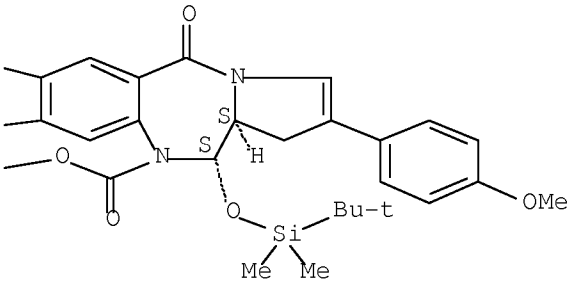
RN 913262-39-2 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-10(5H)-carboxylic acid, 8,8'-[1,5-pentanediylbis(oxy)]bis[11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-11,11a-dihydro-7-methoxy-2-(4-methoxyphenyl)-5-oxo-, bis(2,2,2-trichloroethyl) ester, (11S,11'S,11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
AN 2005:1004748 CAPLUS Full-text
DN 143:306348
TI Preparation of pyrrolobenzodiazepinone derivatives as antitumor agents
IN Howard, Philip Wilson; Gregson, Stephen John
PA Spirogen Limited, UK
SO PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2005085251	A1	20050915	WO 2005-GB768	20050301
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2005219626	A1	20050915	AU 2005-219626	20050301
	CA 2558195	A1	20050915	CA 2005-2558195	20050301
	EP 1720881	A1	20061115	EP 2005-717846	20050301
	R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				
	JP 2007525535	T	20070906	JP 2007-501340	20050301
	US 20070173497	A1	20070726	US 2007-598518	20070206
PRAI	GB 2004-4575	A	20040301		
	GB 2004-26392	A	20041201		
	WO 2005-GB768	W	20050301		

OS CASREACT 143:306348; MARPAT 143:306348
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = labile leaving group, alkenyl or substituted phenyl; R2 and R5 independently = H, OH, SH, etc.; R3 and R4 independently = H, NH2, halo, etc. or the compound is a dimer with each monomer being of formula I, where the R3 and R4 groups of each monomer form together a dimer bridge -X-R-X-; R = alkylene group, which may be interrupted by heteroatoms or aromatic rings; X = O, S or NH; R6 = carbamate-based N-protecting group; R7 = oxygen protecting group or OH or R6 and R7 together form double bond between N10 and C11] and their pharmaceutically acceptable salts, are prepared and disclosed as antitumor agents. Thus, e.g., II was prepared by palladium catalyzed coupling of III (preparation given) with trans-propenylboronic acid followed by deprotection. The in vitro cytotoxicity of I towards K562 human chronic myeloid leukemia cells was evaluated using ELISA assay and it was revealed that selected compds. of the invention displayed IC50 values of less than 1 μM. I should prove useful in the treatment of proliferative diseases such as leukemia. Pharmaceutical compns. comprising I are disclosed.

IT 864754-61-0P 864754-63-2P 864754-66-5P
864754-70-1P 864754-72-3P 864754-74-5P
864754-75-6P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic

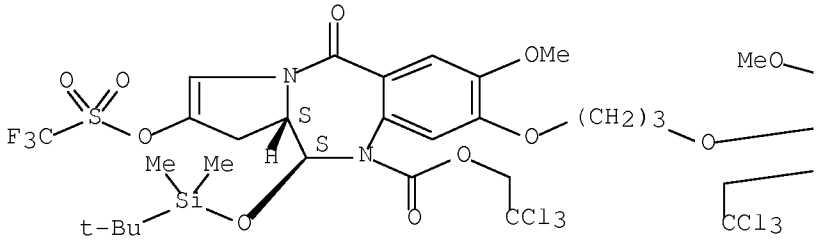
preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyrrolobenzodiazepinone derivs. as antitumor agents)

RN 864754-61-0 CAPLUS

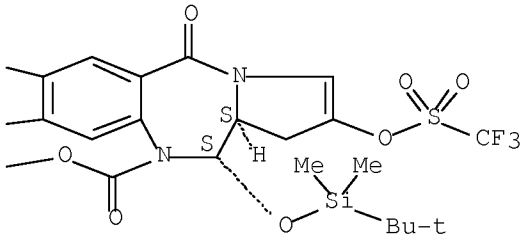
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-10(5H)-carboxylic acid, 8,8'-[1,3-propanediylbis(oxy)]bis[11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-11,11a-dihydro-7-methoxy-5-oxo-2-[[(trifluoromethyl)sulfonyl]oxy]-, bis(2,2,2-trichloroethyl) ester, (11S,11'S,11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

PAGE 1-A



PAGE 1-B

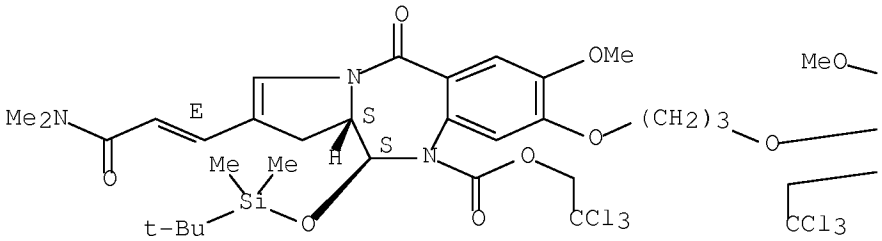


RN 864754-63-2 CAPLUS

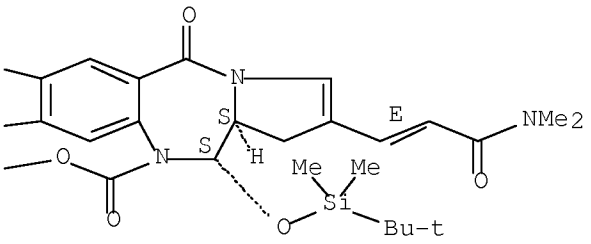
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-10(5H)-carboxylic acid, 8,8'-[1,3-propanediylbis(oxy)]bis[2-[(1E)-3-(dimethylamino)-3-oxo-1-propenyl]-11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-11,11a-dihydro-7-methoxy-5-oxo-, bis(2,2,2-trichloroethyl) ester, (11S,11'S,11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



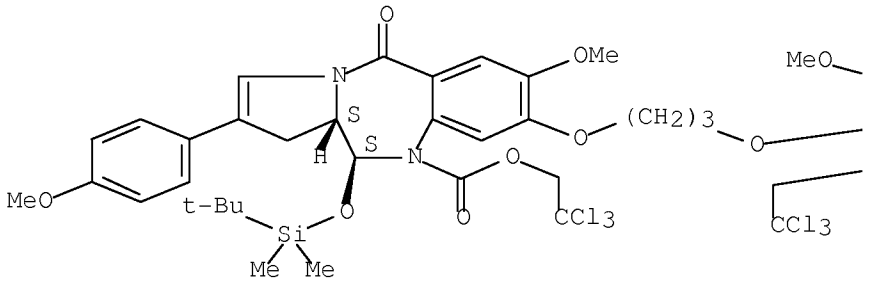
PAGE 1-B



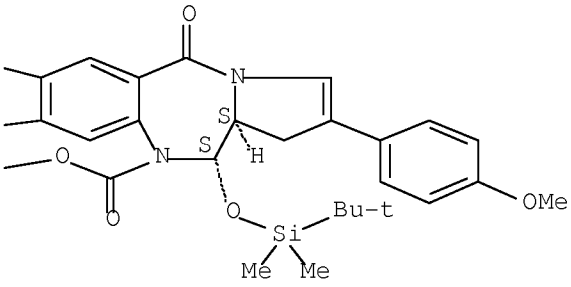
RN 864754-66-5 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-10(5H)-carboxylic acid, 8,8'-[1,3-propanediylbis(oxy)]bis[11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-11,11a-dihydro-7-methoxy-2-(4-methoxyphenyl)-5-oxo-, bis(2,2,2-trichloroethyl) ester, (11S,11'S,11aS,11'aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

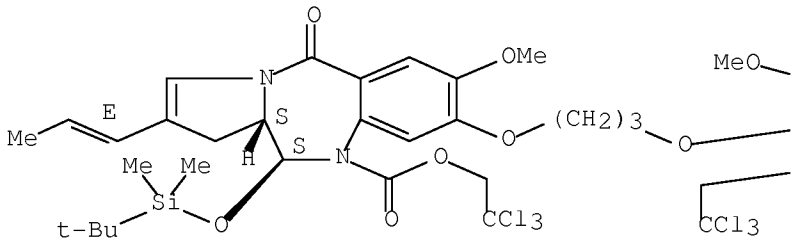


RN 864754-70-1 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-10(5H)-carboxylic acid, 8,8'-[1,3-propanediylbis(oxy)]bis[11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-11,11a-dihydro-7-methoxy-5-oxo-2-(1E)-1-propenyl-, bis(2,2,2-trichloroethyl) ester, (11S,11'S,11aS,11'aS)- (9CI)

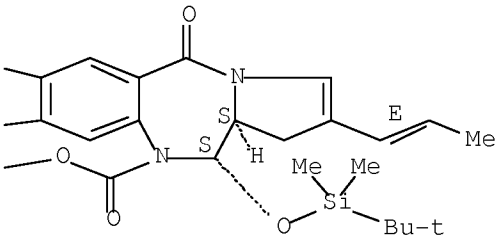
(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

PAGE 1-A



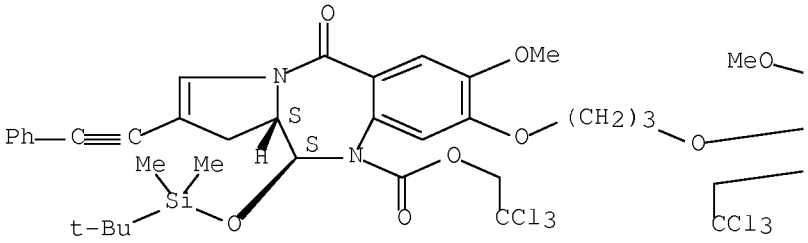
PAGE 1-B

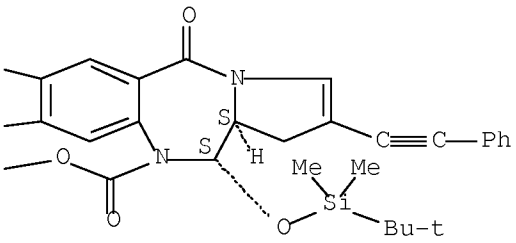


RN 864754-72-3 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-10(5H)-carboxylic acid, 8,8'-[1,3-propanediylbis(oxy)]bis[11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-11,11a-dihydro-7-methoxy-5-oxo-2-(phenylethynyl)-, bis(2,2,2-trichloroethyl) ester, (11S,11'S,11aS,11'aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

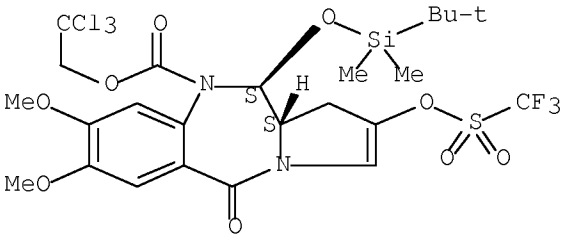
PAGE 1-A





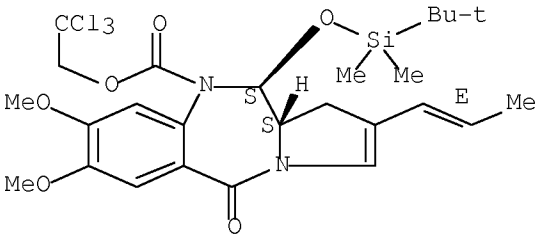
RN 864754-74-5 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-10(5H)-carboxylic acid, 11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-11,11a-dihydro-7,8-dimethoxy-5-oxo-2-[[(trifluoromethyl)sulfonyl]oxy]-, 2,2,2-trichloroethyl ester, (11S,11aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 864754-75-6 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-10(5H)-carboxylic acid, 11-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-11,11a-dihydro-7,8-dimethoxy-5-oxo-2-(1E)-1-propen-1-yl-, 2,2,2-trichloroethyl ester, (11S,11aS)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.

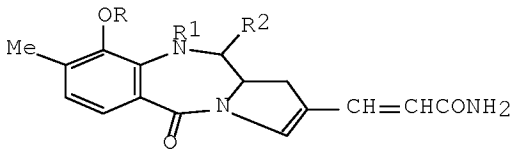


RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1981:139855 CAPLUS Full-text
DN 94:139855
OREF 94:22905a,22908a
TI Benzodiazepines
PA Green Cross Corp., Japan
SO Belg., 24 pp.
CODEN: BEXXAL
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	BE 882305	A1	19800716	BE 1980-199851	19800319
	JP 56015289	A	19810214	JP 1979-89886	19790717
	JP 62037631	B	19870813		
	SE 8001458	A	19810118	SE 1980-1458	19800225
	SE 436882	B	19850128		
	SE 436882	C	19850509		
	CA 1152985	A1	19830830	CA 1980-346511	19800227
	US 4309437	A	19820105	US 1980-127984	19800304
	GB 2053894	A	19810211	GB 1980-8033	19800310
	GB 2053894	B	19830420		
	NL 8001531	A	19810120	NL 1980-1531	19800314
	DE 3010544	A1	19810129	DE 1980-3010544	19800319
	DE 3010544	C2	19820701		
	FR 2461711	A1	19810206	FR 1980-6153	19800319
	FR 2461711	B1	19830513		
	CH 648848	A5	19850415	CH 1980-2187	19800320
PRAI	JP 1979-89886	A	19790717		

OS MARPAT 94:139855
GI
http://www.uspto.gov

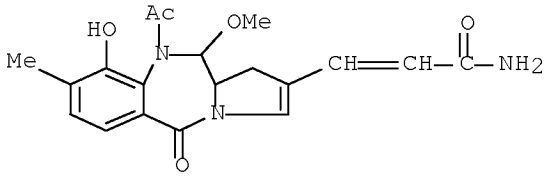


I

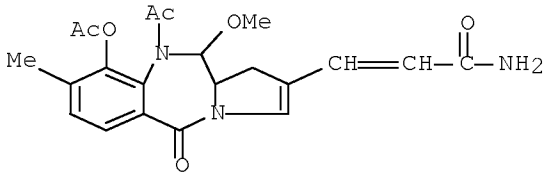
AB Pyrrolobenzodiazepines I (R = H, acyl, CONH2, alkoxycarbonyl; R1 = H, acyl; R2 = SO2H) were prepared by treating I (R2 = OMe) with Na dithionite. I (R2 = SO3H) were prepared by oxidizing I (R2 = SO2H) or by treating I (R2 = OMe) with SO2 or K2SO3. Thus, 1 g I (R = R1 = Ac, R2 = OMe) was treated with Na dithionite to give 0.8 g I (R = R1 = Ac, R2 = SO2H), which at 0.12 mg/kg daily i.p. for 6 days increased the survival time of leukemia P388 infected mice by 190%.

IT 77004-92-3 77004-94-5 77004-97-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(sulfination of)

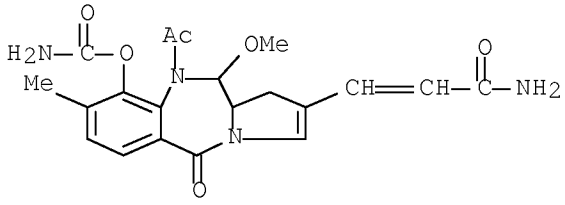
RN 77004-92-3 CAPLUS
CN 2-Propenamide, 3-(10-acetyl-5,10,11,11a-tetrahydro-9-hydroxy-11-methoxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl)- (CA INDEX NAME)



RN 77004-94-5 CAPLUS
CN 2-Propenamide, 3-[10-acetyl-9-(acetyloxy)-5,10,11,11a-tetrahydro-11-methoxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl]- (CA INDEX NAME)



RN 77004-97-8 CAPLUS
CN 2-Propenamide, 3-[10-acetyl-9-[(aminocarbonyl)oxy]-5,10,11,11a-tetrahydro-11-methoxy-8-methyl-5-oxo-1H-pyrrolo[2,1-c][1,4]benzodiazepin-2-yl]- (CA INDEX NAME)



L15 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
AN 1970:531049 CAPLUS Full-text
DN 73:131049
OREF 73:21357a,21360a
TI Antiprotozoal, anthelmintic, and antitumor benzodiazepine compounds
IN Leimgruber, Willy; Schenker, Fausto E.
PA Hoffmann-La Roche Inc.
SO U.S., 13 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

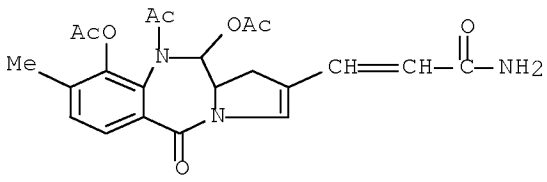
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 3523941	A	19700811	US 1967-620618	19670306
PRAI US 1967-620618	A	19670306		

GI For diagram(s), see printed CA Issue.

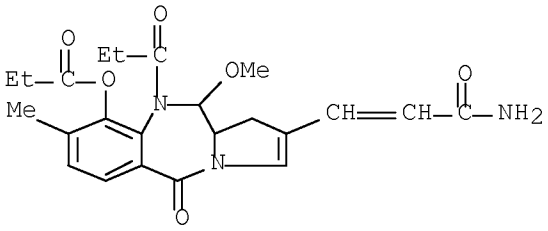
AB The acetates of I and II were prepared by acylation of the corresponding 9-OH derivative I (R1 = R2 = H, R3 = α-OMe) (III), or its hydrate. The epimers of I were prepared by acylating III, removing the elements of MeOH from the mol. by an 8 hr reflux with H2C:C(Me)OAc and treating the product with MeOH at room temperature Thus, III in 1:1 Ac2O-NEt3 stirred 4 hr at 20° gave (11R,11aS)-5,10,11,11a-tetrahydro-9-hydroxy-11-methoxy-8- methyl-5-oxo- 1H-pyrrolo[2,1-c][1,4]benzodiazepine-2-trans-acrylamide acetate (IV). (11S,11aS)-Epimer of IV was similarly prepared and had the same activity against S 180 and Ehrlich solid tumors in mice. II (R1 = H) stirred 2 hr at 20° in 1:1 Ac2O-C5H5N gave II (R1 = Ac) (V). V in 4:1 H2O-Me2CO kept 18 hr at 20° gave I (R1 = H, R2 = Ac, R3 = OH) (VI). V in C5H5N kept 3 days at 20° in AcOH-Ac2O gave I (R1 = R2 = Ac, R3 = AcO). Treatment of III.H2O with (EtCO)2O-NEt3, (PrCO)2O-NEt2, or Bz3O-NEt3 gave I (R1 = EtCO, PrCO, or Bz). Similar acylations of III.H2O with PhNCO, EtNCO, or (EtO)2CO in the presence of NEt3 gave I (R1 = PhNHCO, EtNHCO, EtCO2). I are useful as antitumor agents against Sarcoma 180 and Ehrlich solid tumors in mice, as antiprotozoal agents against Entamoeba histolytica and Trichomonas vaginalis, and as anthelmintic agents against Syphacia obvelata.

IT 29455-46-7P 29455-48-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

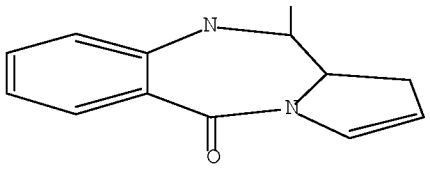
RN 29455-46-7 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2-acrylamide, 10-acetyl-5,10,11,11a-tetrahydro-9,11-dihydroxy-8-methyl-5-oxo-, diacetate (ester), (E)-(S,S)-(+)- (8CI) (CA INDEX NAME)



RN 29455-48-9 CAPLUS
CN 1H-Pyrrolo[2,1-c][1,4]benzodiazepine-2-acrylamide, 5,10,11,11a-tetrahydro-9-hydroxy-11-methoxy-8-methyl-5-oxo-10-propionyl-, propionate (ester), (E)-(11R,11aS)- (8CI) (CA INDEX NAME)

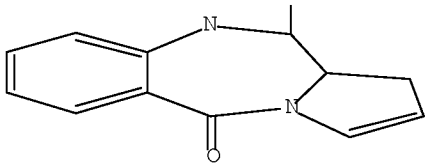

O
Et
C
O
Et
C
O
OMe
Me
N
CH
CH
C
O
NH2
N
O

=> d l2; d l6; d l11; d his; log y
L2 HAS NO ANSWERS
L1 STR



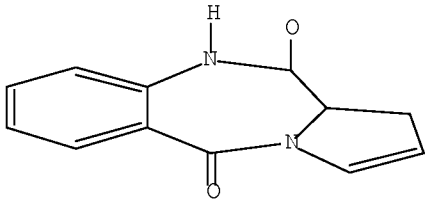
Structure attributes must be viewed using STN Express query preparation.
L2 QUE ABB=ON PLU=ON L1

L6 HAS NO ANSWERS
L5 STR



Structure attributes must be viewed using STN Express query preparation.
L6 QUE ABB=ON PLU=ON L5

L11 HAS NO ANSWERS
L10 STR



Structure attributes must be viewed using STN Express query preparation.
L11 QUE ABB=ON PLU=ON L10

(FILE 'HOME' ENTERED AT 10:40:14 ON 11 MAR 2009)

FILE 'REGISTRY' ENTERED AT 10:41:15 ON 11 MAR 2009
L1 STRUCTURE UPLOADED
L2 QUE L1
L3 8 S L2
L4 215 S L2 FUL
L5 STRUCTURE UPLOADED
L6 QUE L5
L7 5 S L6 SAM SUB=L4
L8 145 S L6 FUL SUB=L4
L9 70 S L4 NOT L8
L10 STRUCTURE UPLOADED
L11 QUE L10
L12 2 S L11 SAM SUB=L9
L13 49 S L11 FUL SUB=L9
L14 21 S L9 NOT L13

FILE 'CAPLUS' ENTERED AT 10:45:45 ON 11 MAR 2009
L15 5 S L14

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	29.20	306.88

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-4.10	-4.10

STN INTERNATIONAL LOGOFF AT 10:46:51 ON 11 MAR 2009